N-ACYL- AND N-ALKYL-SUBSTITUTED ETHYLENEUREAS

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UDC 547.783:541.69

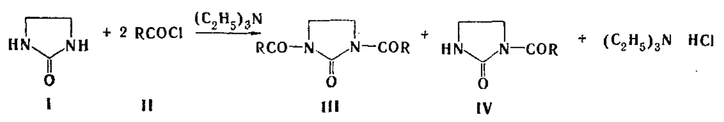
A number of N-acyl- and N-alkyl derivatives of ethyleneurea were synthesized, and their repellent activity was studied.

Urea derivatives are attracting ever-increasing attention as biologically active compounds. Many of them find practical application as pesticides [1]. Tetraalkyl-substituted ureas have repellent properties. In particular, bis-N,N-hexamethylenecarbamide ("carboxide") has been proposed instead of N,N-diethyl-m-toluamide as a repellent with longer-lasting action [2].

In order to search for new preparations that have repellent activity, we obtained a series of N,N'-diacyl and N,N'-dialkyl derivatives of ethyleneurea (2-imidazolidone).

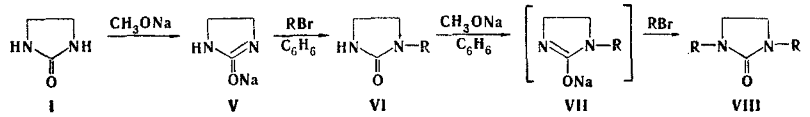
N,N'-Diacetyl and N,N'-dipropionylethyleneureas were previously synthesized by refluxing ethyleneurea with acid anhydrides [3]. Some N,N'-dialkylethyleneureas were obtained by cyclization of symmetrically substituted ethylenediamine with phosgene [4, 5] or urea [6].

We obtained N,N'-diacetyl and N,N'-dipropionyl derivatives of ethyleneurea by refluxing the latter with acid chlorides of the appropriate acids. We were unable to carry out a similar reaction with the chlorides of higher acids because of pronounced resinification. However, acylation did proceed in the presence of triethylamine:



In this case, monoacylation products IV (Table 1) are formed in addition to N,N'-diacyl derivatives III, and the relative amount of them in the mixture increases as the acyl residue becomes heavier. Absorption bands were observed at 1700-1710 cm^{-1} (ring C=O) and 1750-1770 cm^{-1} (acyl residue C=O) in the IR spectra of the diacyl derivatives. In addition, the spectra of the monoacyl derivatives have an absorption band at 3200-3300 cm^{-1} (N−H).

N,N'-Dialkyl- and N-monoalkylethyleneureas were obtained by alkylation of the sodium salt of ethyleneurea with alkyl bromides (Table 2):



Shchelkovskii Branch, All-Union Scientific-Research Institute of Chemical Agents for the Protection of Plants. S. M. Kirov Military Medical Academy. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 90-93, January, 1973. Original article submitted December 20, 1971.

TABLE 1. Acyl Derivatives of Ethyleneurea

R	mp, °C*	R_f	Empirical formula	Found, %			Calc., %			Yield, %
				C	H	N	C	H	N	
N,N'-Diacyl derivatives III										
CH_3	125—126	0,55	$C_7H_{10}N_2O_3$	—	—	—	—	—	—	73
C_2H_5	135—136†	0,55	$C_9H_{14}N_2O_3$	54,8	7,1	14,4	54,5	7,1	14,1	60
C_3H_7	53—54	0,60	$C_{11}H_{18}N_2O_3$	58,3	7,9	12,8	58,4	8,0	12,4	60
C_4H_9	37—38	0,70	$C_{13}H_{22}N_2O_3$	61,5	8,7	11,3	61,4	8,7	11,0	67
C_5H_{11}	36—37	0,70	$C_{15}H_{26}N_2O_3$	64,4	9,6	9,8	63,8	9,3	9,9	79
C_6H_{13}	42—43	0,70	$C_{17}H_{30}N_2O_3$	65,6	10,0	9,1	65,5	9,7	9,0	61
C_7H_{15}	48—49	0,70	$C_{18}H_{34}N_2O_3$	67,1	10,2	8,5	67,4	10,1	8,3	57
C_8H_{17}	64—65	0,75	$C_{21}H_{38}N_2O_3$	68,5	10,7	7,5	68,8	10,5	7,6	62
C_9H_{19}	61—62	0,80	$C_{23}H_{42}N_2O_3$	70,2	10,7	7,1	70,0	10,7	7,1	36
$C_6H_5CH{=}CH$	253—254	0,70	$C_{21}H_{18}N_2O_3$	73,3	5,3	8,1	72,8	5,3	8,1	32
N-Acyl derivatives IV										
C_7H_{15}	85—86	0,35	$C_{11}H_{20}N_2O_2$	62,1	9,9	13,2	62,2	9,5	13,2	29
C_8H_{17}	88—89	0,35	$C_{12}H_{22}N_2O_2$	63,8	9,9	12,4	63,7	9,8	12,4	31
C_9H_{19}	91—92	0,35	$C_{13}H_{24}N_2O_2$	65,2	10,2	11,7	64,9	10,1	11,6	56
$C_6H_5CH{=}CH$	198—199	0,25	$C_{12}H_{12}N_2O_2$	67,1	5,8	13,1	66,6	5,6	12,9	12

*The diacyl derivatives were crystallized from alcohol, and the monoacyl derivatives were crystallized from hexane.

† Literature data [3]: mp 115-120°C.

It is known that sodium salts of heterocycles that contain an amide grouping of atoms have the enol structure [7]. By analogy, we adopted structure V for the sodium salt of ethyleneurea. The absorption band at 1610 cm^{-1} characteristic for the C=N bond was actually observed in the IR spectrum of the salt that we obtained. Because of the extremely poor solubility of ethyleneurea in neutral organic solvents, we were unable to obtain this salt in pure form, and unchanged sodium methoxide was therefore usually present in the reaction mixture during its alkylation. Due to it, the initially formed N-monoalkylethyleneurea (VI) is capable of forming salt VII, which is further alkylated to form N,N'-dialkylethyleneurea VIII.

We showed that N,N'-dialkylethyleneurea actually can be obtained by the reaction of N-monoalkylethyleneurea VI with alkyl bromide in the presence of sodium methoxide in benzene; this confirms the possibility of the intermediate formation of sodium salt VII under the reaction conditions and, consequently, the stepwise character of the alkylation of ethyleneurea.

An absorption band at 1700-1710 cm^{-1} (C=O) was observed in the IR spectra of N,N'-dialkylethyleneureas, but the characteristic absorption for the NH group at 3200-3300 cm^{-1} was absent. Both of the indicated absorption bands are present in the IR spectra of N-monoalkyl derivatives.

The repellent properties of the compounds obtained were studied by the method in [8] with C. tesquorum. The acyl derivatives of ethyleneurea and a large portion of the alkyl derivatives proved to be inactive. Satisfactory repellent properties were observed for hexyl-, dibutyl-, and diamylethyleneureas. N,N'-Diheptylethyleneurea is close to N,N-diethyl-m-toluamide in repellent activity.

EXPERIMENTAL

The starting ethylenediamine was distilled twice over KOH. The course of the separation and the degree of purity of the compounds obtained were monitored by thin-layer chromatograph (TLC) on activity II aluminum oxide in a benzene–acetone (4 : 1) system in the case of acyl derivatives and in acetone in the case of alkyl derivatives of ethyleneurea (development with iodine vapors). The IR spectra of films and KBr pellets were recorded with a UR-10 spectrometer.

Ethyleneurea (I). This compound was obtained by a modification of the method in [10]. A 23.6-g (0.2 mole) sample of diethyl carbonate was added to 13.4 ml (0.2 mole) of ethylenediamine, and the mixture was heated at 175-180° until the distillation of ethanol ceased. It was then cooled, and the residue was recrystallized from chloroform to give 15.8 g (92%) of a substance with mp 129-130° (mp 131° [10]).

Acylation of Ethyleneurea. A 0.1-mole sample of the carboxylic acid chloride was added at 0° to a mixture of 0.05 mole of ethyleneurea (I) and 0.1 mole of trimethylamine in 40 ml of toluene, the temperature was gradually raised to room temperature, and the mixture was heated at 90-100° for 5 h. Water (50 ml) was added, the organic layer was separated, and the aqueous layer was extracted with toluene. The combined extracts were washed with 5% hydrochloric acid and water and dried with magnesium sulfate. The toluene was removed by distillation, and the residue was vacuum fractionated and recrystallized. In

TABLE 2. Alkyl-Substituted Ethyleneureas

R	bp (mm) or mp, °C	d_4^{20}	n_D^{20}	MR_D		R_f	Empirical formula	Found, %			Calc., %			Yield, %
				found	calc.			C	H	N	C	H	N	
N, N'-Dialkyl derivatives VI														
CH_3	60—61 (1,0)[a]	1,0468	1,4720	30,53	30,32	0,70	$C_5H_{10}N_2O$	52,8	8,9	24,3	52,6	8,9	24,5	29
C_2H_5	84—85 (3,0)[b]	0,9960	1,4691	39,77	39,56	0,75	$C_7H_{14}N_2O$	59,0	10,1	19,7	59,1	9,9	19,7	30
C_3H_7	97—98 (1,0)[c]	0,9633	1,4671	49,05	48,76	0,80	$C_9H_{18}N_2O$	63,2	11,1	16,0	63,5	10,7	16,4	27
C_4H_9	119—120 (0,8)[d]	0,9435	1,4659	58,21	58,03	0,80	$C_{11}H_{22}N_2O$	66,1	11,2	13,7	66,6	11,2	14,1	33
C_5H_{11}	110—111 (0,3)	0,9283	1,4660	67,54	67,27	0,80	$C_{13}H_{26}N_2O$	69,5	11,8	12,5	69,0	11,6	12,4	26
C_6H_{13}	139—140 (0,5)	0,9197	1,4664	76,68	76,50	0,85	$C_{15}H_{30}N_2O$	70,6	12,0	10,9	70,8	11,9	11,0	27
C_7H_{15}	159—160 (0,6)	0,9122	1,4672	85,96	85,75	0,85	$C_{17}H_{34}N_2O$	72,2	12,1	9,8	72,3	12,1	9,9	34
C_8H_{17}	170—171 (0,5)[e]	0,9067	1,4676	95,05	94,97	0,85	$C_{19}H_{38}N_2O$	73,4	12,1	9,0	73,5	12,4	9,0	18
C_9H_{19}	181—183 (0,5)	0,9036	1,4680	104,17	104,21	0,90	$C_{21}H_{42}N_2O$	74,4	12,4	8,3	74,5	12,5	8,3	42
$C_{10}H_{21}$	26—27	—	—	—	—	0,90	$C_{23}H_{46}N_2O$	75,1	12,6	7,7	75,3	12,7	7,7	28
N-Alkyl derivatives VII														
C_2H_5	48—50	—	—	—	—	0,40	$C_5H_{10}N_2O$	52,7	9,2	24,5	52,6	8,8	24,5	39
C_3H_7	109—110 (1,0)	1,0478	1,4807	34,79	34,94	0,40	$C_6H_{12}N_2O$	56,4	9,6	21,4	56,2	9,5	21,8	51
C_4H_9	30—31	—	—	—	—	0,40	$C_7H_{14}N_2O$	59,3	9,8	19,2	59,1	9,9	19,7	37
C_5H_{11}	29—30	—	—	—	—	0,40	$C_8H_{16}N_2O$	61,2	10,4	17,9	61,5	10,3	17,9	38
C_6H_{13}	141—142 (0,5)	0,9902	1,4764	48,54	48,79	0,45	$C_9H_{18}N_2O$	63,0	10,7	16,4	63,5	10,7	16,4	33
C_7H_{15}	27—28	—	—	—	—	0,45	$C_{10}H_{20}N_2O$	65,2	11,1	15,3	65,2	11,0	15,2	36
C_8H_{17}	38—39	—	—	—	—	0,45	$C_{11}H_{22}N_2O$	66,6	11,2	14,0	66,6	11,2	14,1	30
C_9H_{19}	55—56	—	—	—	—	0,45	$C_{12}H_{24}N_2O$	67,7	11,4	13,1	67,9	11,4	13,2	18

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[a] bp 106-108° (17 mm) [9]. [b] bp 122° (22 mm) [5]. [c] bp 148° (23 mm) [5]. [d] bp 137-140° (3 mm) [6].
[e] bp 195-200° (3 mm) [6].

the case of cinnamyl derivatives, the mixture of mono- and diacylation products was separated by chromatography on activity II aluminum oxide. N,N'-Dicinnamylethyleneurea was eluted with benzene, while N-cinnamylethyleneurea was eluted with benzene–acetone (19:1). The yields, physical constants, and analyses of the substances are presented in Table 1. All of the compounds obtained are colorless, odorless, crystalline substances that are insoluble in water and soluble in ether and benzene.

N,N-Diacetylethyleneurea. A mixture of 4.3 g (0.05 mole) of ethyleneurea (I), 50 ml of absolute toluene, and 7.85 g (0.1 mole) of acetyl chloride was refluxed for 6 h, after which the solvent was removed by distillation, and the residue was recrystallized from alcohol to give 6.22 g (73%) of a substance with mp 125-126°. N,N'-Dipropionylethyleneurea (see Table 1) was similarly obtained.

Alkylation of Ethyleneurea. A 0.1-mole sample of ethyleneurea (I) was added to a solution of sodium methoxide (0.1 g-atom* of sodium in 50 ml of absolute methanol), and the mixture was refluxed for 6 h. The alcohol was removed by distillation, and the residual white crystalline mass was heated in vacuo at 120° for 2 h. A solution of 0.3 mole of alkyl bromide in 75 ml of absolute benzene was added to the resulting sodium salt of ethyleneurea, and the mixture was refluxed with stirring for 8 h, after which the precipitate was removed by filtration. The benzene was removed by distillation, and the residue was chromatographed with a column filled with activity II aluminum oxide and then distilled. N,N'-Dialkylethyleneurea VIII was eluted with benzene–acetone (9:1), while N-alkylethyleneurea VI was eluted with benzene–acetone (1:1). The yields, physical constants, and analyses of the substances are presented in Table 2. The alkyl derivatives of ethyleneurea are insoluble in water but soluble in the usual organic solvents.

Alkylation of N-Nonylethyleneurea. A solution of 3.1 g (15 mmole) of nonyl bromide in 5 ml of absolute benzene was added by drops to a mixture of 0.27 g (5 mmole) of sodium methoxide and 1.0 g (4.7 mmole) of N-nonylethyleneurea in 10 ml of absolute benzene. The precipitate was removed by filtration, the benzene was removed by distillation, and the residue was chromatographed with a column filled with activity II aluminum oxide and distilled to give 1.3 g (31%) of N,N'-dinonylethyleneurea with bp 180-182° (0.5 mm) and n_D^{20} 1.4676.

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*The yield of dialkylethyleneurea remained almost the same when the amount of sodium was doubled.